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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/517,275	MIN ET AL.	
	Examiner	Art Unit	
	Kimberly Chong	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-61* is/are pending in the application.

4a) Of the above claim(s) *1-21,23,25,26,28-46,49-52,54 and 58-60* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22,24,27,47,48,53,55-57,61* is/are rejected.

7)☒ Claim(s) *22,27,53,55-57 and 61* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/18/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 11/20/2007 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 05/21/2007 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 11/20/2007, claims 1-54 and new claims 55-61 are pending in the application. Applicant has pointed out to Examiner that claim 53 is directed to a method of treatment of an autoimmune disease and is within the scope of previously examined claim 47 and therefore should have been examined along with claim 47. After further consideration, claim 53 is in fact within the scope of claim 47 and will be examined along with the elected claims as well as new claims 55-57 and 61. Claims 1-21, 23, 25, 28-46, 49-52, 54 and new claims 58-60 are withdrawn as being drawn to a non-elected invention.

Information Disclosure Statement

The information disclosure statement filed on 10/18/2007 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because of the following reasons: The foreign patent document having numbers AU2003209308 has not been considered because the document is not made of record and appears to not have been filed.

New Claim Objections and Rejections

Claim Objections

Claims 22, 27, 47, 48, 53, 55, 56, 57 and 61 are objected to as reciting non-elected subject matter. Claims 22, 27, 47, 48, 53, 55, 56, 57 and 61 should be rewritten deleting any non-elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 47, 48, 53, 55-57 and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 47, 48, 53, 55-57 and 61 are drawn to method for decreasing immunogenicity and rejection potential of an organ for transplantation, said method comprising perfusing into said organ at least one construct that suppresses T-cell activity and inhibits the expression of an endogenous target gene encoding a cytokine, wherein the construct is an siRNA.

The specification as filed discloses siRNA molecules targeted to IL-12 and IFN-gamma (Example 2). The specification discloses prophetic methods of inhibiting

cytokines to treat a variety of immune disorders (see pages 23-25). The specification does not provide adequate written description of a construct that targets any cytokine wherein this construct suppresses T cell function and further treatment of transplant rejection of any organ in a mammalian subject. The specification does not provide adequate written description of any siRNA molecule that targets any cytokine such that T cell suppression occurs and further provides treatment of transplantation rejection of any organ in any mammalian subject.

The specification fails to provide any structure or sequence that would impart the recited activity of inhibition of any cytokine expression such that T cell suppression and treatment of transplant rejection of any organ occurs. Further, the specification does not provide any specific examples or an adequate number of species to represent the claimed genus of constructs capable of inhibition of any cytokine.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

MPEP 2163 states in part, "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916,

927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")

Thus, the instantly claimed invention cannot be said to have been adequately described in a way that would convey with reasonable clarity to those skilled in the art that, as of the filling date sought, applicant was in possession of the claimed invention because the specification, while providing information on several siRNA molecules targeted to IL2 and IFN gamma, does not provide any other information or guidance as to what construct or what siRNA construct targeted to any cytokine sequence would inhibit cytokine expression and further suppress T cell activity such that treatment of transplantation rejection occurs.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 57 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 57 recites the limitation "said immune disorder". There is insufficient antecedent basis for this limitation in the claim because claim 55, from which claim 57 depends, recites an "autoimmune disorder". For purposes of prior art, claim 57 will be interpreted to mean an autoimmune disorder such as transplant rejection and therefore will be examined as such.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 47 and 55 are rejected under 35 U.S.C. 102(b) as being anticipated by Qu et al. (Transplantation 2001, Vol. 72(5): pages 915-923 in the journal and pages 1-17 as the included pdf copy).

The instant claim is drawn to a method for decreasing immunogenicity and rejection potential of an organ for transplantation, said method comprising perfusing into said organ at least one construct that suppresses T cell activity, wherein said construct inhibits the expression of an endogenous target gene encoding a cytokine.

Qu et al. teach an antisense compound targeted to a gene encoding an IL-2 protein (Table 1). Qu et al. teach said antisense compound was capable of inhibiting expression from said IL-2 gene (see page 9) and teach injection of said antisense compound intravenously into mice transplanted with an allograft heart (see page 8). The instant specification does not define "perfusing said organ" and therefore for purposes of prior art, perfusing is interpreted to mean the antisense compound is spread through or over the heart, as in by injection intravenously such that the antisense compound is spread to the heart and heart tissue via the blood. Qu et al. teach the mice with the transplanted heart had extended survival of the transplanted organ when administered an antisense compound targeted to IL-12 (see page 12). Qu et al. further teach said antisense compound targeted to IL-2 was capable of decreasing T cell proliferation (see page 12 and Figure 8).

Thus, Qu et al. anticipates claims 47 and 55 of the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 47-48, 53, 55-57 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Qu et al. (Transplantation 2001, Vol. 72(5): pages 915-923 in the

journal and pages 1-17 as the included pdf copy) as applied to claims 47 and 55 above and in view of Hammond et al. (Nature Reviews Genetics February, 2001 cited on PTO 892 mailed 05/21/2007) and Tuschl et al. (WO 02/44321 cited on PTO 892 mailed 05/21/2007).

The instant claims are drawn to a method for decreasing immunogenicity and rejection potential of an organ for transplantation, said method comprising perfusing into said organ at least one construct that suppresses T cell activity, wherein said construct inhibits the expression of an endogenous target gene encoding a cytokine, wherein the construct is a siRNA and wherein the immune disorders is transplant rejection.

Qu et al. is relied upon as above. Qu et al. do not teach a siRNA molecule targeted to a cytokine gene.

Hammond et al. teach two methods for silencing specific genes: antisense and RNA interference. Hammond et al. teach that although antisense methods are straightforward techniques for probing gene function, the methods have suffered from "...questionable specificity and incomplete efficacy." (see page 110, column 1). Hammond et al. further teach " "...dsRNAs have been shown to inhibit gene expression in a sequence-specific manner" and further "RNAi is a potent method, requiring only a few molecules of dsRNA per cell to silence expression."

Tuschl et al. teach siRNA molecules and teach compositions comprising siRNA and an acceptable carrier that are capable of silencing gene expression (see page 9, lines 17-25). Tuschl et al. teach siRNA molecules can be delivered in expression

constructs (se page 7). Tuschl et al. teach that siRNAs represent a new alternative to antisense or ribozyme therapeutics.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a siRNA molecule, as taught by Hammond et al. and Tuschl et al. to target a gene encoding Il-2 cytokine, as taught by Qu et al.

One would have been motivated to use a siRNA targeted to an IL-2 cytokine gene and inhibit gene expression because Qu et al. teach inhibition of IL-2 cytokine expression leads to extended survival of organ transplantation. One would have been motivated to use a siRNA targeted to an IL-2 cytokine gene instead of an antisense because it was well known at the time the invention was made that siRNA molecules are efficient molecules to target and decrease expression of a target gene and because Hammond et al. teach using siRNA to inhibit gene expression is more sequence specific than using antisense methodologies and RNAi using dsRNA is a more potent method requiring only a few molecules of dsRNA per cell. One would have been motivated to create such compounds with increased stability and functionality, and since siRNAs are taught by Tuschl et al. as being useful in silencing gene expression.

One would have a reasonable expectation of success given that Tuschl et al. teach how to make and use virtually any siRNA to any gene provided the target sequence is known and teach that methods of RNA synthesis are known in the art, as evidenced by the examples provided therein.

Thus in the absence of evidence to the contrary, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Response to Applicant's Arguments

Re: Sequence Compliance

Acknowledgement is made of amendment to the specification inserting the required sequence identifiers on pages 27-28 and therefore the application now complies with the with the requirements of 37 CFR 1.821 through 1.825.

Re: Claim Rejections - 35 USC § 101 and 35 USC § 112

The rejection of claims 22, 24 and 27 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for the reasons of record in the action mailed 05/21/2007.

The rejection of claims 22, 24 and 27 under 35 U.S.C. 101 is maintained for the reasons of record in the action mailed 05/21/2007.

Applicant's arguments filed 11/20/2007 have been fully considered but they are not persuasive. Applicant argues claims 22, 24 and 27 are directed to the use of a composition of matter and do not need to be defined in terms of an active method or process step.

To the contrary, the recitation of "the use " in the claims implies the claims are drawn to a method or process and as stated in the previous Office action, it is unclear what method and/or process applicant is intending to encompass. A claim is indefinite

where it merely recites a use without any active, positive steps delimiting how this use is actually practiced and further the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process.

Thus, the rejection of record is maintained.

Re: Claim Rejections - 35 USC § 102

The rejection of claim 47 under 35 U.S.C. 102(e) as being anticipated by Keshavjee et al. (US 2003/0180301) is withdrawn in view of the new grounds of rejection above, however Keshavjee et al. was applied as a proper 102(e) reference, contrary to Applicant's arguments. Applicant argues Keshavjee et al. has a filing date of January 21, 2003 and a publication date of September 25, 2002 both of which occur well after the June 10, 2002 date of the priority date of the present application. Applicant is correct in noting the filing date and publication date of Keshavjee et al., however Keshavjee et al. has an effective filing date of January 22, 2002, which is before the June 10, 2002 priority date of the instant application. Therefore, Keshavjee et al. was applied as a proper 102(e) reference.

Re: Claim Rejections - 35 USC § 103

The rejection of claims 47-48 under 35 U.S.C. 103(a) as being unpatentable over Keshavjee et al. as applied to claim 47 above, and further in view of Hammond et al. (Nature Reviews Genetics February, 2001) and Tuschl et al. (WO 02/44321) is withdrawn in view of the new grounds of rejection above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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/Kimberly Chong/
Examiner
Art Unit 1635